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Primary Cardiac Lymphoma

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Primary cardiac lymphoma is a rare entity. We report on the clinicopathological features of 2 patients with primary cardiac lymphomas: one involving the right atrium resulting in intractable right heart failure, and the other involving the pericardium with massive pericardial effusion. In the first patient, sternotomy and surgical biopsy of the tumor were performed to arrive at the diagnosis. In the second patient, CT thorax and transesophageal echocardiography helped to diagnose the pericardial tumor, and cytological examination of the pericardial fluid established the pathological diagnosis of lymphoma. Combination chemotherapy (COPP) was started in both patients. The first patient died on the first day of chemotherapy due to intractable heart failure, while the second attained a partial response to chemotherapy but died of progressive disease 8 weeks later. This is followed by a literature review of 21 patients with primary cardiac lymphoma. In conclusion, the prognosis of primary cardiac tumor remains poor. Am. J. Hematol. 54:79–83, 1997

Key words: primary cardiac lymphoma; pathological diagnosis; prognosis

INTRODUCTION

Primary cardiac tumors involving the pericardium and/or myocardium are rare. Primary cardiac lymphoma is described as a lymphoma involving only the heart and/or pericardium, or with the main bulk of disease localized to the heart. Patients may present with signs of heart failure, cardiac tamponade, or arrhythmias, depending on the site of the tumor. These tumors often give rise to a clinical emergency requiring urgent diagnosis and prompt treatment. However, although the diagnosis of cardiac tumors has been facilitated by the use of modern imaging, access to the tumor for histological diagnosis of the malignant lymphoma remains difficult, owing to the absence of peripheral lymph node involvement. As a result, diagnosis is late and often only made postmortem, imparting a poor prognosis to primary cardiac lymphoma. Nevertheless, cytological examination of the pericardial and pleural fluid has resulted in early diagnosis of the malignant lymphoma without need for open biopsy of the tumor, thus allowing early treatment in some reports [15,16,18]. In this article, the clinicopathological features of 2 Chinese patients with primary B-cell non-Hodgkin's lymphoma of the heart are presented, one with a huge right atrial tumor obstructing the tricuspid flow, and the other with a pericardial tumor with pericardial effusion. Also, the application of modern imaging technology and the cytological examination of body fluids in early diagnosis of the cardiac tumor and in defining the nature of the malignant lymphoma are illustrated. This is followed by a review of the English literature of the disease from 1960 onwards [3–19].

CASE REPORTS

Patient 1

The first patient was a 69-year-old woman who enjoyed good past health until 4 weeks prior to admission, when she developed progressive shortness of breath on exertion. She also noticed progressive increase in puffiness of face, abdominal distension, sweating, and ankle edema. Physical examination showed patient was tachypnoeic with puffiness of face and bilateral pitting ankle edema to midshin. Blood pressure was 100/60 mm Hg, and pulse was 100/min with elevated jugular venous pressure. There was no peripheral lymphadenopathy or hepatosplenomeg-

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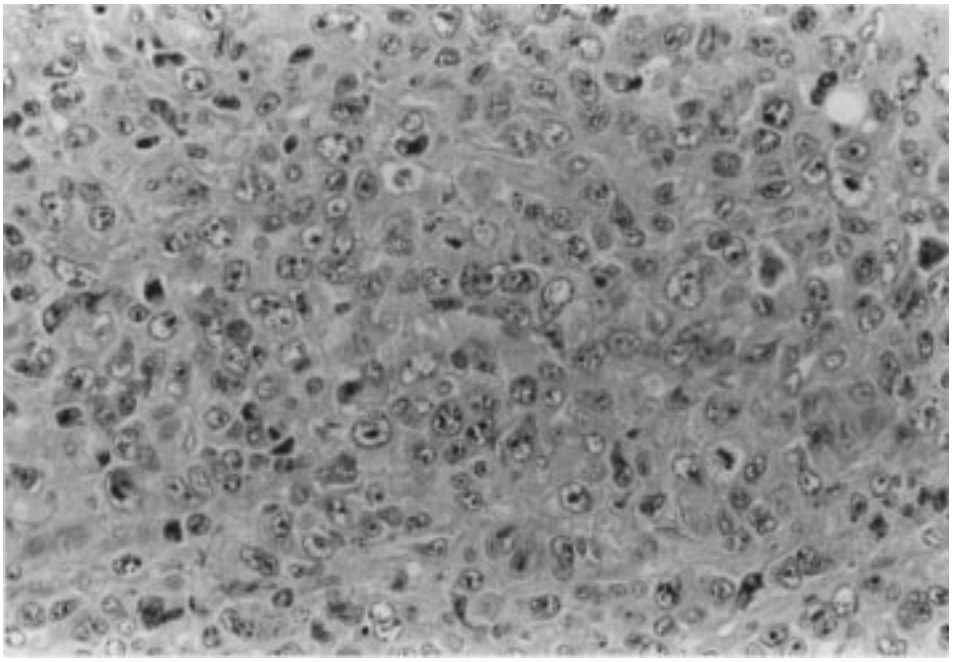

Fig. 1. Biopsy of heart tumor of patient 1, showing diffuse infiltration by large, round lymphoid cells with vesicular chromatin and multiple nucleoli (B5 fixation, hematoxylin-eosin, ×500).

TABLE I. Patients' Characteristics and Laboratory Results*

	Patient 1	Patient 2
Sex	F	F
Age	69	68
Site of tumor	Right atrium	Pericardium
Diagnosis by:	Sugery	Cytology
Complete blood picture		
Hemoglobulin (g/l)	12.5	12
Leukocyte count ($\times 10^9$/l)	9.4	12
Platelet count ($\times 10^9$/l)	389	195
LDH (u/l)	536	1,478
Liver function test		
Albumin (g/l)	38	30
Globulin (g/l)	26	35
Alkaline phosphatase (u/l)	107	125
Bilirubin (umol/l)	31	58
SGPT (u/l)	73	27
SGOT (u/l)	36	75
GGT (u/l)	30	92

*Normal ranges: hemoglobin, 12–18 g/l; leukocyte count, 4–11 $\times 10^9$/l; platelets, 150–400 $\times 10^9$/l; albumin, 44–56 g/l; globulin, 24–36 g/l; bilirubin, 7–19 umol/l; LDH, 200–360 u/l; alkaline phosphatase, 34–104 u/l; SGPT, 5–31 u/l; SGOT, 12–28 u/l; GGT, 7–30 u/l.

aly. CT scan of the thorax showed a right atrial tumor but no mediastinal lymphadenopathy. Transesophageal echocardiogram revealed a 6 × 5 cm tumor abutting on the lateral wall of the right atrium, obstructing the tricuspid valve. During sternotomy, a firm and fleshy tumor was seen growing out from the right atrial/right ventricular groove. Incisional biopsy showed diffuse large-cell lymphoma (Fig. 1). The lymphoma cells were positive for the B-cell marker CD20, but negative for T-cell markers CD3, CD45RO, and CD30. Blood tests results are shown in Table I. CT scan of the abdomen did not reveal any intraabdominal disease, and bilateral trephine biopsies were clear of lymphoma cells. COPP (cyclophosphamide 450 mg/m^2/day on days 1 and 8, vincristine 2 mg/m^2/day on days 1 and 8, procarbazine 100 mg/m^2/day for 2 weeks, and prednisone 40 mg/m^2/day for 2 weeks) at 50% dosage was started, but the patient died on the day of treatment.

Patient 2

A 68-year-old woman enjoyed good health until 2 months prior to admission, when she developed progressive shortness of breath and decrease in effort tolerance. She had a low-grade fever of 37.5°C, but there was no peripheral lymphadenopathy or hepatosplenomegaly. Blood pressure was 120/65 mm Hg; pulse was 100/min; jugular venous pressure was mildly raised. Electrocardiogram showed sinus tachycardia with a rate of 100/min and low voltage. Transthoracic echocardiogram showed a significant pericardial effusion, with a tumor measuring 4 × 2 cm, abutting on the pericardium. CT thorax showed tumor in the pericardial sac invading into the right ventricle, pericardial effusion, and a left pleural effusion without mediastinal lymphadenopathy (Fig. 2). CT scan of the abdomen did not reveal any intraabdominal lymph node enlargement. Pericardiocentesis yielded 500 ml of

Fig. 2. CT scan of thorax, showing tumor nodules in the pericardial sac, pericardial effusion, and left pleural effusion.

bloodstained fluid, and a pleural tap showed bloodstained pleural fluid. Cytological examination of both specimens revealed plentiful large round cells with coarse chromatin and prominent nucleoli (Fig. 3). The cells were positive for the B-cell marker CD 20, but not for the T-cell markers CD3 and CD45RO. Bilateral trephine biopsies did not reveal any evidence of disease. Blood test results are shown in Table I. COPP (dosage as listed in patient 1) at 50% dosage was started, and the patient had gradual resolution of symptoms and the effusions disappeared. A repeat CT scan of the thorax after the second course of chemotherapy showed a 50% reduction of the pericardial tumor. However, 8 weeks after diagnosis, the patient was admitted because of shortness of breath. Examination showed that patient was ill-looking, confused, and tachypneoic. Blood pressure was 100/60 mm Hg, pulse was 100/min, jugular venous pressure was raised, and there was fine crepitation at the lung bases. There was no peripheral lymp node enlargement or any hepatosplenomegaly. Transthoracic echocardiogram and CT scan of the thorax confirmed recurrence of the pericardiac tumor. LDH was 2,000 u/l (N:200–360 u/l). Lumbar puncture was performed in view of the unexplained mental status, and cerebrospinal fluid was sent for cytological examination, which revealed lymphoma cells similar to those found in the pleural and pericardial fluid. IMVP (ifosfamide lg/m^2/day for 5 days, methotrexate 30 mg/m^2/day on days 3 and 10, and etoposide 100 mg/m^2/day on days 1–3) and intrathecal methoxate were given. Despite salvage chemotherapy, the patient deteriorated and died 2 weeks later. The patient's family refused postmortem examination.

DISCUSSION

Primary cardiac lymphoma is rare: only 7 cases were reported in the Armed Forces Institute of Pathology [1]. In the Western literature, up to 1960, approximately 35 cases of malignant lymphoma were found among 178 malignant cardiac tumors [3,20,21]. In a local study, in a review of 12,485 autopsies over a 20-year period, there were only 7 cases of primary cardiac tumors with an autopsy incidence of primary cardiac tumors of 0.056%, and yet none of the 7 was a malignant lymphoma [2]. In a similar study of primary tumors of the heart over a 31-year period, there were 30 malignant tumors, of which only 3 were malignant lymphoma [22]. We reviewed the primary cardiac lymphomas reported in English from 1960 onwards (Table II): all of them were only case reports, reflecting the rarity of this entity, which made a systematic analysis difficult.

Patient 1 presented with intractable right heart failure, while patient 2 presented with pleural effusion and mas-

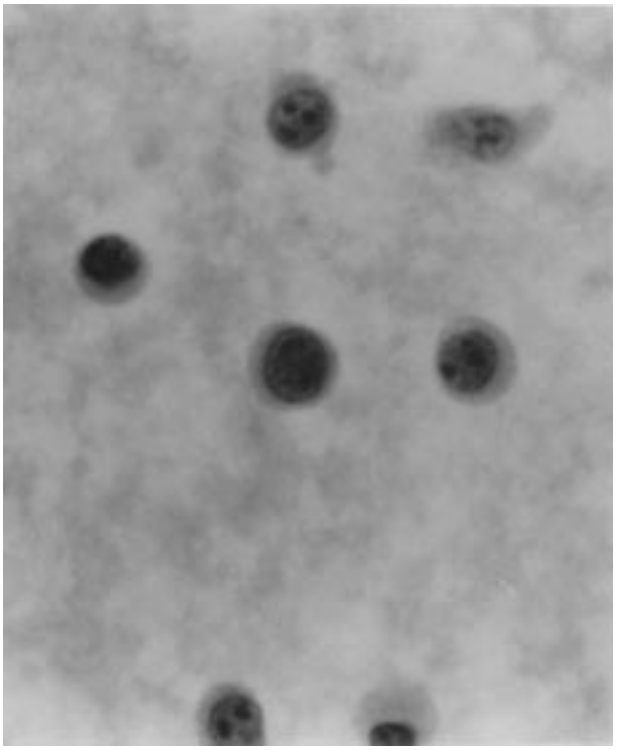

Fig. 3. Cytology specimen of pericardial fluid of patient 2, showing scattered large, round lymphoid cells with vesicular chromatin and multiple nucleoli (ethanol fixations, Papanicolaou stain, ×1,000).

sive pericardial effusion. These are common presentations in primary cardiac lymphoma, as shown in Table II.

The diagnosis of a cardiac tumor was made in our patients with the help of echocardiogram and was also confirmed with CT scan. In earlier reports, the diagnosis of a cardiac tumor was usually made postmortem, and thus no specific treatment could be offered. The proper pathological diagnosis of malignant lymphoma is essential in order to administer appropriate treatment. In patient 1, open biopsy established the diagnosis of malignant lymphoma. In patient 2, the pericardial fluid revealed abnormal lymphoma cells, so that diagnosis of malignant lymphoma was possible without tissue histology, and specific treatment could be offered. In the literature, only 9 patients had the diagnosis made antemortem with cytological examination of the pericardial fluid in 5 [7,11,15,16,18], surgical biopsy in 2 [17,19], pericardial biopsy during pericardiocentesis in 1 [14], and myocardial biopsy during cardiac catheterisation in 1 [4]. This showed that cytological examination is a valuable diagnostic tool in cardiac lymphoma, especially when open biopsy of the tumor is often difficult due to critical clinical status. In doubtful cases, it was also possible to define the clonal nature of the lymphoid cells in the centesis fluid by polymerase chain reaction of the immunoglobulin heavy chain gene [23].

TABLE II. Characteristics of 21 Patients Reviewed in the Literature

Patient number	21
M/F	17/4
Median age (years)	39.5
Immune defect	
AIDS	7 (33%)
Renal transplantation	2 (9%)
Signs and symptoms	
Onset	1 day–4 months
Pericardial effusion	10 (47%)
Pleural effusion	10 (47%)
Heart failure	13 (62%)
Cardiac tamponade	5 (24%)
Arrhythmia	7 (33%)
Superior Vena Cava Syndrome	1 (5%)
Site of tumor	
Pericardium	3 (14%)
Peri- and myocardium	2 (9.5%)
Myocardium	16 (76%)
Right ventricle	12 (57%)
Right atrium	10 (48%)
Left ventricle	8 (38%)
Interventricular septum	2 (9%)
Left atrium	2 (9%)
Diagnosis made postmortem	
Of cardiac tumor	8 (38%)
Of malignant lymphoma	12 (57%)
Method of tissue diagnosis	
Myocardial biopsy	1
Cytology	6
Surgery	2
Pericardectomy	1
Tissue	
Histology specified type	19 (90%)
Lymphosarcoma	3
Diffuse large-cell	12
Immunoblastic	4
Lineage	
B	10
Not specifed	9
Specific treatment	7
Chemotherapy	5
Radiotherapy	1
Both	1
Complete remission (CR)	5
CR duration (months)	4–40

Both of our patients had large-cell lymphoma of the B lineage. Of the 21 patients reviewed, 12 patients were reported as diffuse large-cell, and 4 as immunoblastic. Of the 9 cases with immunophenotype of the tumor reported, all belonged to the B lineage. Thus, primary cardiac lymphoma is mainly a B-cell lymphoma of diffuse large-cell type (working formulation).

Patient 1 had a right atrial tumor. Preference of right-sided involvement in primary cardiac lymphoma is common, in contrast to left-side predominance in atrial myxoma, which is the major primary benign cardiac tumor.

Patient 2 had quite a drastic initial response to our combination chemotherapy in terms of symptoms, and imaging showed a 50% reduction of tumor size. Our patient unfortunately had rapid progression of disease after 2 months, with reaccumulation of pericardial effusion, and also central nervous system (CNS) disease, as documented by cytological examination of the cerebrospinal (CSF). In the reviewed patients, specific treatment was given in 7, and complete remission was documented in only 5 [14–16,18,19].

In conclusion, although primary cardiac lymphoma is a rare entity, antemortem pathological diagnosis is still difficult, and prognosis remains poor.

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